

WHAT IS CLAIMED IS:

1. A sustained-release pharmaceutical composition in a form of an orally deliverable tablet comprising an active pharmaceutical agent having solubility not less than about 10 mg/ml, dispersed in a matrix comprising a hydrophilic polymer and a starch having a tensile strength of at least about 0.15 kN cm⁻² at a solid fraction representative of the tablet.
2. The composition of Claim 1 wherein the starch has a tensile strength of at least about 0.175 kN cm⁻² at a solid fraction representative of the tablet.
3. The composition of Claim 1 wherein the starch has a tensile strength of at least about 0.2 kN cm⁻² at a solid fraction representative of the tablet.
4. The composition of Claim 1 wherein the starch is a pregelatinized starch.
5. The composition of Claim 1 wherein the starch is present in an amount of about 25% to about 75% by weight.
6. The composition of Claim 1 wherein the starch is present in an amount of about 40% to about 70% by weight.
7. The composition of Claim 1 wherein the starch is present in an amount of about 45% to about 65% by weight.
8. The composition of Claim 1 wherein the hydrophilic polymer is selected from the group consisting of methylcellulose, hydroxypropylmethylcellulose, carmellose sodium and carbomer.
9. The composition of Claim 1 wherein the hydrophilic polymer is hydroxypropylmethylcellulose.
10. The composition of Claim 1 wherein the hydrophilic polymer is present in an amount of about 20% to about 70% by weight.
11. The composition of Claim 1 wherein the hydrophilic polymer is present in an amount of about 30% to about 60% by weight.
12. The composition of Claim 1 wherein the hydrophilic polymer is present in an amount of about 35% to about 50% by weight.
13. The composition of Claim 1 wherein the active pharmaceutical agent has solubility

- not less than about 50 mg/ml.
14. The composition of Claim 1 wherein the active pharmaceutical agent has solubility not less than about 100 mg/ml.
 15. The composition of Claim 1 wherein the active pharmaceutical agent is therapeutically effective at a daily dose not greater than about 100 mg.
 16. The composition of Claim 1 wherein the active pharmaceutical agent is therapeutically effective at a daily dose not greater than about 50 mg.
 17. The composition of Claim 1 wherein the active pharmaceutical agent is therapeutically effective at a daily dose not greater than about 25 mg.
 18. The composition of Claim 1 wherein the active pharmaceutical agent is therapeutically effective at a daily dose not greater than about 10 mg.
 19. The composition of Claim 1 wherein the active pharmaceutical agent is therapeutically effective at a daily dose not greater than about 5 mg.
 20. The composition of Claim 1 wherein the active pharmaceutical agent is a CNS agent.
 21. The composition of Claim 20 wherein the CNS agent is selected from the group consisting of anticonvulsants, antidepressants, antidyskinetics, antiepileptics, antimanics, antimigraine agents, antimuscarinics, antiobsessionals, antiparkinsonian agents, antipsychotics, antispasmodics, anxiolytics, cholinergics, CNS stimulants, dopamine receptor agonists, dopamine receptor antagonists, hypnotics, monoamine oxidase inhibitors, neuroleptics, neuroprotectives, NMDA receptor antagonists, nootropics, prolactin inhibitors, sedatives, selective serotonin reuptake inhibitors, selective noradrenaline reuptake inhibitors, serenics, serotonin receptor agonists, serotonin receptor antagonists and tranquilizers.
 22. The composition of Claim 20 wherein the active pharmaceutical agent is a salt of reboxetine or an enantiomer thereof.
 23. The composition of Claim 22 wherein the active pharmaceutical agent is (S,S)-reboxetine succinate.
 24. The composition of Claim 22 that comprises about 0.2 to about 15 mg reboxetine per tablet.

25. The composition of Claim 22 that comprises about 1 to about 12 mg reboxetine per tablet.
26. The composition of Claim 1, further comprising a coating on the tablet.
27. The composition of Claim 26 wherein said coating is a release-controlling layer.
28. The composition of Claim 27 wherein said release-controlling layer constitutes about 1% to about 15% by weight of the tablet.
29. The composition of Claim 26 wherein said coating is a nonfunctional coating.
30. A pharmaceutical composition in a form of an orally deliverable tablet comprising (S,S)-reboxetine succinate in an amount of about 1, 2, 4, 6, 8 or 12 mg base equivalent, dispersed in a matrix comprising (a) HPMC type 2208 in an amount of about 35% to about 50% by weight of the tablet and (b) a pregelatinized starch having a tensile strength of at least about 0.15 kN cm^{-2} at a solid fraction of 0.8, in an amount of about 45% to about 65% by weight of the tablet.
31. A method of treatment of a subject having a condition or disorder for which an active pharmaceutical agent having solubility not less than about 10 mg/ml is indicated, the method comprising orally administering to the subject the pharmaceutical composition of Claim 1.
32. The method of Claim 31 wherein the composition is administered not more than once daily.
33. The method of Claim 31 wherein said condition or disorder is a CNS condition or disorder selected from the group consisting of paranoid, schizoid, schizotypal, bipolar, histrionic, delusional, narcissistic, emotionally unstable, psychopathic and sociopathic personality disorders; habit and impulse disorders; obsessive-compulsive disorder; passive-aggressive disorder; acute and transient psychotic disorders; psychotic depression; schizoaffective disorder; hypochondria; cyclothymia; dysthymia; manic-depressive illness; major depressive disorder; treatment-resistant depression; adult and childhood onset schizophrenias; harmful use and abuse of, addiction to or dependence on opioids, narcotics, barbiturates, alcohol, benzodiazepines, amphetamines, cocaine, cannabinoids, hallucinogens, stimulants, nicotine (tobacco), other drugs and solvents; withdrawal states and mood and psychotic disorders related to drug dependence; sexual dysfunction; gender

identity disorders; sexual preference disorders; general anxiety disorder; social anxiety disorder; mixed anxiety and depressive disorder; attention deficit hyperactivity disorder and depression and anxiety associated therewith; depression, anxiety, emotional dysregulation and behavioral disturbances associated with mental retardation; developmental disorders; childhood conduct and attachment disorders; premenstrual dysphoric disorder; postpartum depression; phobias; posttraumatic stress disorder; dissociative disorder; Briquet's syndrome; affective disorders; organic mood, anxiety and emotionally labile disorders resulting from brain damage or dysfunction; chronic fatigue; stress-induced psychotic episodes; presenile dementia, Pick's disease, vascular dementia, multi-infarct dementia, Alzheimer's disease, dementia associated with Creutzfeldt-Jakob disease, HIV-related dementia and other dementias; Parkinson's disease; Huntington's disease; suicidal behavior; eating disorders; adjustment disorders; somatization disorder; somatoform autonomic dysfunction; somatoform pain disorder; panic attacks; panic disorder; amnesia; neuropathic pain; fibromyalgia; migraine; epilepsy; tinnitus; enuresis; sleep disorders; delirium; postconcussion syndrome; multiple sclerosis; tremors; muscular spasms; restless legs syndrome; Lennox-Gastaut syndrome; motor and vocal tic disorders; Tourette's syndrome; supranuclear palsy; Shy-Drager syndrome; trigeminal neuralgia; Bell's palsy; motor neuron diseases such as amyotrophic lateral sclerosis; and psychosomatic and psychosocial conditions associated with non-CNS diseases.

34. The method of Claim 33 wherein the CNS condition or disorder is depressive illness or neuropathic pain and the active pharmaceutical agent is a selective noradrenaline reuptake inhibitor.
35. The method of Claim 34 wherein the selective noradrenaline reuptake inhibitor is (S,S)-reboxetine succinate.
36. A method for determining suitability of a starch for use in a sustained-release orally deliverable tablet comprising an active pharmaceutical agent having solubility not less than about 10 mg/ml, the method comprising the steps of
 - (a) preparing compacts of a sample of the starch on an automated tablet press at a range of compression forces applied for a dwell time of at least about 4 seconds;
 - (b) measuring hardness of each compact, expressed as the force required to cause

crushing of the compact;

(c) determining solid fraction of each compact;

(d) calculating tensile strength σ_T of each compact from the equation

$$\sigma_T = 2F/\pi DH$$

where F is the force required to cause crushing, D is diameter of the compact and H is thickness of the compact;

(e) establishing relationship of tensile strength to solid fraction of the compacts; and

(f) using said relationship to estimate tensile strength at a solid fraction representative of a desired sustained-release tablet;

the starch being deemed suitable for said use if its tensile strength as so estimated is at least about 0.15 kN cm^{-2} .

37. A process for preparing a sustained-release pharmaceutical composition in a form of an orally deliverable tablet, the process comprising selecting by a suitable test a starch having a tensile strength of at least about 0.15 kN cm^{-2} at a solid fraction representative of the tablet; admixing with the selected starch a hydrophilic polymer and an active pharmaceutical agent having solubility not less than about 10 mg/ml to provide a mixture wherein the agent is dispersed in a matrix comprising the polymer and the starch; and compressing the mixture to form said tablet.